REMARKS

Claim Status

Claims 1-17, 19-33, 37 and 38 are pending in this application and stand rejected. Claims 13, 14, 17, 33 and 38 are canceled herein without prejudice. Claims 1, 3, 16, 31 and 37 are amended herein, and new claims 42 and 43 have been introduced. Support for the claim amendments and new claims is provided by the specification at, e.g., page 7, lines13-18; page 10, lines 15-21; page 31, lines 18-25; page 33, lines 3-7; page 34, lines 13-17; and throughout the Examples. Accordingly, no new matter is added by way of these amendments. Applicants respectfully request entry of the claim amendments and new claims, and reconsideration in view of the following remarks.

Formal Matters

Applicants thank Examiner Fay for the courtesy of an interview between the Examiner and the undersigned, participating telephonically, and Kawai Lau, Registration No. 44,461 (representative of the assignee at interest, QLT Inc.), appearing in person, on April 13, 2010 to discuss the status of this case. A response to the substance of interview was submitted by the Applicants on May 3, 2010. This Supplemental Amendment is filed in response to helpful discussions with the Examiner during the interview.

The interview included discussion of Applicants' view that the invention was unexpected because the inflammation caused by normal dose PDT was being treated by the combined, total dose of normal dose PDT plus low dose PDT. The situation is somewhat analogous to the well known situation of using digitalis (digoxin) in heart disease, where a low dose of digitalis (or digoxin) can treat congestive heart failure and a high dose can cause immediate heart failure. But if heart failure is caused by the higher dose, a low (normally therapeutic) dose is useless as treatment.

The claimed invention is based on a surprising result when compared to the digitalis situation. In the instant case, low dose PDT can treat inflammation and a high dose PDT can cause

inflammation, but unlike digitalis, that resultant inflamed tissue can be treated successfully with follow-on low dose PDT! Because this surprising effect was not known at the time of the invention, Applicants have had trouble understanding the difficulties encountered by the claims. Examiner Fay indicated that she understood Applicants' view and suggested that Applicants should consider claim revisions and remarks to present the view for further consideration.

Rejections under 35 U.S.C. § 103

Claims 1-17, 19-33, 37 and 38 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over WO 98/34644, for reasons of record, in view of Chen (U.S. 6,602,274). Briefly, WO 98/34644 is said to disclose that low dose PDT can be used to reduce inflammation in injured or pre-injured tissues, and Chen is said to disclose that PDT causes damage to normal tissues beyond the treated area. Applicants traverse the rejections for reasons of record, as well as at least the following reasons.

Independent claim 1 is amended herein to clarify that the area treated with low dose PDT in step b) of the method encompasses (i.e., includes) the target tissue that is treated with normal dose PDT in step a). Independent claim 31 is similarly amended to clarify that the area treated with low dose PDT in step d) encompasses (i.e., includes) the treatment area that is treated with normal dose PDT. Therefore, the claims cannot be mistakenly construed to mean that the low dose PDT is delivered only to a "doughnut" shaped area around the target tissue.

Thus, it will be understood that the "target tissue" in claim 1 and the "treatment area" in claim 31 are exposed to a total light dosage that is the sum of light administered in both the normal dose and the low dose PDT treatment steps. This total dosage is necessarily significantly higher than the dosage of the low dose PDT treatment alone. Both claims 1 and 31, as amended, clearly require that the target tissue (claim 1) or treatment area (claim 31) is exposed to a total light dose that is the sum of the normal dose PDT and the low dose PDT, which is necessarily significantly higher than that of low dose PDT alone.

WO 98/34644 describes appropriate irradiation conditions for low dose PDT as: irradiation at a dose of less than 15 J/cm^2 applied between 0-3 hours after administration of the photosensitizer, when significant amounts of the photosensitizer would still be expected to be present (page 36, lines 24-25). Irradiation at light doses up to 100 J/cm^2 is described when irradiation is applied later than 6 hours after photosensitizer administration, at which time most of the photosensitizer would be expected to have been cleared (page 36, lines 26-27). Particularly preferred conditions for use during surgery are said to include exposing the treated tissue to about 7-12 J/cm^2 of light (page 37, line 20).

In addition, WO 98/34644 at page 40, lines 3-9 states that: "The data indicated that a certain level of PDT was required, but that higher doses were generally less effective than lower ones. The combination of the short incubation time with BPD and the low light dosage of 12 J/cm^2 was not expected to cause much damage to treated cells. Nevertheless, the treatment had a definite pharmacological action. Bleb survival was associated with the lack of inflammation, as indicated by avascularity and a pale-colored bleb."

The data presented in Table 1A and 1B on page 39 of WO 98/34644 shows that irradiation above 12 J/cm^2 resulted in vascularity, and poor bleb survival, indicators of inflammation (see, e.g., Table 1A and B, rabbit nos. 5 and 6, treated with 18 and 24 J/cm^2, respectively).

Applicants respectfully submit that these statements and data would have suggested to one of ordinary skill that there is a maximum PDT dose that will provide the anti-inflammatory effect and that at higher irradiation doses, inflammation occurs. Taken as a whole, WO 98/34644 suggests that irradiation at a dose of less than 15 J/cm^2 would be preferred, and that irradiation at higher light doses did not provide anti-inflammatory efficacy.

As amended, both claims 1 and 31 require that the target tissue (claim 1) or treatment area (claim 31) is exposed to a total light dose that is higher than the low dose PDT indicated by WO 98/34644. In view of the disclosure of WO 98/34644, one of ordinary skill in the art would not have reasonably believed that irradiation at a total light dose greater than the low dose PDT reported

by WO 98/34644 would have provided the anti-inflammatory effects described by the cited reference at lower light doses.

Accordingly, Applicants respectfully submit that one of skill in the art would not have had a reasonable expectation of success that the instantly claimed methods would be effective to reduce or prevent inflammation in a treated subject. To the contrary, Applicants submit that a skilled person would be surprised at the discovery of reduced inflammation by using a total combined PDT dose that exceeds the low dose PDT reported in WO 98/34644. Applicants further submit that in view of the lack of a reasonable expectation of success and the unexpected nature of the invention, no basis has been provided to explain why one of skill in the art would have made the modifications to the cited art necessary to achieve the instant invention.

In view of the foregoing remarks, Applicants respectfully request that the rejections under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 273012011800. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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By: / Leslie A. Robinson /
Leslie A. Robinson
Registration No.: 54,403
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
(858) 314 7692